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Anthony Giaccio, Esq.  
KENYON & KENYON  
One Broadway  
INew York, NY 10004

EXAMINER

COLLINS, CYNTHIA E

ART UNIT PAPER NUMBER

1638

DATE MAILED: 07/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/978,273

Applicant(s)

THOMAS ET AL.

Examiner

Cynthia Collins

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 22 March 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 38-54 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 38-54 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

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## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed on March 22, 2005 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 22, 2005 has been entered.

Claims 1-37 are cancelled.

Claims 38-54 are newly added.

Claims 38-54 are pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

### ***Claim Rejections - 35 USC § 112***

Claims 38 and 41-54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record.

Applicants' arguments filed March 22, 2005 have been fully considered but they are not persuasive.

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Applicants maintain that support for the claimed invention can be found on p. 9, line 19, through p. 11, line 5, of the specification which discloses SEQ ID NO.: 2 and the stringent hybridization conditions that may be used to isolate additional sequences encoding a protein having ribosome inactivating activity. Furthermore, the working examples of the specification describe the actual isolation of a nucleic acid encoding a maize ribosome inactivating protein as well as the use of assays for confirmation that the isolated nucleic acid molecule encodes a protein with ribosome inactivating activity. Applicants submit that, given the teachings of the specification of both structural and functional features of the ribosome inactivating proteins encompassed by the claims, a sufficient written description has been provided. (reply pages 6-7)

The rejection is maintained because the genus of sequences recited in the claims is not adequately described. The outstanding rejection was not predicated on a lack of support for the stringent hybridization conditions that may be used to isolate additional sequences encoding a protein having ribosome inactivating activity; the rejection was predicated on a lack of description of additional sequences encoding a protein having ribosome inactivating activity. Applicants have described only a single sequence that codes for a maize type 3 ribosome inactivating protein (SEQ ID NO:2) and its parts (the  $\alpha$  domain and the  $\beta$  domain, separated by a central peptide spacer and flanked by N and C terminal peptides). Applicants have not described other sequences that code for a protein having type 3 ribosome inactivating protein activity. Applicants have not described a representative number of sequences that are homologous to SEQ ID NO:2 and that encode polypeptides that retain the activity of a type 3 ribosome inactivating protein. Applicants also have not described the structural features of SEQ ID NO:2 that would be

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retained by homologous sequences that encode polypeptides that retain the activity of a type 3 ribosome inactivating protein. Absent a description of a representative number of functional species or the structural features of functional species, the genus of sequences recited in the claims is not described.

Claims 38-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing a transgenic Solanaceous plant transformed with a chimaeric gene comprising a coding sequence of SEQ ID NO:2 encoding a recombinant mature maize ribosome inactivating protein comprising an  $\alpha$  domain and a  $\beta$  domain arranged contiguously, the expression of which inactivates the plant's ribosomes, does not reasonably provide enablement for a method of producing a transgenic Solanaceous plant transformed with a chimaeric gene comprising a coding sequence having 70-90% homology to SEQ ID NO:2 or encoding any unspecified protein having type 3 ribosome inactivating activity, the expression of which causes any unidentified type of plant cytotoxicity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, for the reasons of record.

Applicants' arguments filed March 22, 2005 have been fully considered but they are not persuasive.

Applicants maintain that, as indicated above, support for the claimed invention can be found on p. 9, line 19, through p. 11, line 5, of the specification which discloses SEQ ID NO.: 2 and the stringent hybridization conditions that may be used to isolate

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additional sequences encoding a protein having ribosome inactivating activity.

Furthermore, Applicants point out that the working examples of the specification describe the actual isolation of a nucleic acid molecule encoding a maize ribosome inactivating protein as well as the use of assays for confirmation that the isolated nucleic acid molecule encodes a protein with ribosome inactivating activity. Applicants maintain that given that the specification discloses SEQ ID NO.: 2 and the stringent hybridization conditions, including working examples which describe assays for detecting ribosome inactivating activity, coupled with the knowledge of the skilled artisan at the time the invention was filed, undue experimentation would not have been required by one of skill in the art to develop and evaluate methods for generating the transgenic solanaceous plants encompassed by the claims. (reply pages 7-8)

The Examiner maintains that the outstanding rejection was not predicated on a failure to provide guidance with respect to the employment of methods that are known to and within the abilities of one skilled in the art, such as techniques for hybridization and for detecting ribosome inactivating activity. The outstanding rejection was predicated on a failure to provide sufficient guidance with respect to how to distinguish between those sequences that would have the desired effect upon expression in a transgenic plant and those that would not, as the effect of expressing only a single type of ribosome inactivating protein obtained from a single species of plant is exemplified. Such guidance is necessary because the effect of expressing a chimaeric gene comprising a coding sequence having 70-90% homology to SEQ ID NO:2 or binding to SEQ ID NO:2 under stringent hybridization conditions or encoding any unspecified protein having type 3 ribosome inactivating activity is unpredictable, because even though different ribosome

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inactivating proteins share structurally similar regions, they vary in their ability to inactivate ribosomes.

The outstanding rejection was also predicated on a failure to provide sufficient guidance with respect to which non-Solanaceous plant ribosomes would be susceptible to inactivation by the protein encoded by SEQ ID NO:2, as only effects on Solanaceous plants are exemplified. Such guidance is necessary because the effect of expressing a chimaeric gene comprising a coding sequence of SEQ ID NO:2 in a wide variety of different plant species is unpredictable because plant ribosomes from different plant species exhibit different levels of susceptibility to different ribosome inactivating proteins.

The outstanding rejection was additionally predicated on a failure to provide sufficient guidance with respect to which cytotoxic effects other than ribosome inactivation to screen for, as only methods for determining the effect of expressing SEQ ID NO:2 on ribosome inactivation are disclosed. Such guidance is necessary because the ability of a chimaeric gene comprising a coding sequence of SEQ ID NO:2 to produce plant cytotoxic effects other than ribosome inactivation upon expression is unpredictable, since plant cells can be subject to cytotoxic effects that involve a variety of different cellular structures and processes and that are mediated by a variety of different mechanisms.

With regard to the Examiner's comments concerning transgenic plants transformed with chimeric genes further comprising transcriptional or translational enhancer sequences and/or intracellular targeting sequences and introns, and/or

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nucleotide sequences operable to facilitate the transformation process and stable expression of the chimeric gene, the examiner is reminded that a patent need not teach, and preferably omits, what is well known in the art. In re Buchner, 929 F.2d 660 (Fed. Cir. 1991). Applicants assert that since transcriptional and translational enhancer sequences, intracellular targeting sequences, intron sequences, nucleotide sequences that facilitate the transformation process and stable expression of the chimeric gene are all well known to those of skill in the art, undue experimentation would not have been required by one of skill in the art to develop chimeric genes containing such elements. (reply page 8)

The Examiner maintains that the use of the claimed sequences in combination with type 3 ribosome inactivating protein coding sequences for the purpose of causing plant cell cytotoxicity by ribosome inactivation at a desired target site it is not well known in the art. In the absence of further guidance, undue experimentation would be required by one skilled in the art to select from among the numerous diverse sequences available those particular sequences that, when included as part of a chimaeric gene encoding a maize ribosome inactivating protein, would function in concert with the chimaeric gene to cause plant cytotoxicity at a target site in the same manner as the chimaeric gene exemplified.

***Claim Rejections - 35 USC § 102***

Claims 38, 41-47 and 49-54 are rejected under 35 U.S.C. 102(b) as being anticipated by Maddaloni et al. (Transgenic Research, 1997, Vol. 6, No. 6, pages 393-402), for the reasons of record.



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Applicants' arguments filed March 22, 2005 have been fully considered but they are not persuasive.

Applicants maintain that Maddaloni does not anticipate the presently claimed invention as Maddaloni fails to describe the selective expression of a ribosome inactivating protein to a specific location within the plant body, i.e., a target site for induction of plant cell death at that location. (reply page 9)

In response to Applicants' argument that Maddaloni et al. fail to show certain features of Applicants' invention, it is noted that the features upon which Applicants rely (i.e., the selective expression of a ribosome inactivating protein to a target site for induction of plant cell death at that location) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The Examiner further maintains that the recitation in the preamble of claims 38, 51 and 52 that the expression of the chimeric gene "causes plant cell cytotoxicity by ribosome inactivation at a desired target site within the plant body", "causes plant cytotoxicity" or "causes plant cytotoxicity at a target site" does not distinguish the claimed invention from Maddaloni, as these limitations are intended uses or end results of practicing the claimed invention. The methods of claims 38, 41-47 and 49 require only the transformation of any unspecified type of plant cells with a chimeric gene comprising a promoter which is induced at and/or adjacent to any unspecified desired target site, said promoter being operably linked to a nucleic acid which encodes a protein having type 3 ribosome inactivating activity. Maddaloni et al. teach the transformation of tobacco plant

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cells with a chimeric gene comprising a potato wun1 promoter that is induced by wounding at, and or adjacent to, a wounding target site, said promoter being operably linked to a nucleic acid which encodes a protein having type 3 ribosome inactivating activity. Accordingly the method taught by Maddaloni et al. anticipates the claimed method. Further, because the method taught by Maddaloni et al. utilizes the exact same materials and method steps as are recited in the rejected claims, the method taught by Maddaloni et al. is presumed to produce the same end result as the claimed method, i.e. "cause plant cell cytotoxicity by ribosome inactivation at a desired target site within the plant body", or "cause plant cytotoxicity at a target site".

With respect to claims 53-54, the Examiner also notes that the claims are silent with respect to the effect of expressing the nucleic acid molecule. With respect to claim 51, the Examiner maintains that the expression of the coding sequence taught by Maddaloni et al. would inherently cause some level of plant cytotoxicity, because the maize ribosome inactivating protein has the inherent ability to inactivate heterologous plant ribosomes, including tobacco ribosomes.

Applicants also point out that ribosome inactivating proteins are known to be potent inhibitors of protein translation, and that the present invention is directed to the use of ribosome inactivating proteins in a plant cell death system wherein selective gene expression of ribosome inactivating proteins to a targeted location within a transgenic plant, i.e. a target site, leads to plant cell death at that location. Applicants point to the disclosure in the specification that such selective expression of ribosome inactivating proteins may have multiple uses, and Applicants assert that although Maddaloni discloses

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the expression of a maize ribosome-inactivating protein in tobacco under the control of the potato wunl gene promoter, Maddaloni's tobacco plants were not designed to target plant cell death, but rather to target fungal cell death, as is demonstrated by Maddaloni's statement that a major factor limiting the potential activity of ribosome inactivating proteins as plant defensive molecules is related to the ability of such proteins to enter the fungal cell wall." (p. 400, column 2, lines 2-5). (reply pages 9-10)

In response to Applicants' argument that Maddaloni et al. fail to show certain features of Applicants' invention, it is noted that the features upon which Applicants rely (i.e., the use of ribosome inactivating proteins in a "plant cell death system" wherein selective gene expression of ribosome inactivating proteins to a targeted location within a transgenic plant "leads to plant cell death at that location") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Further, because the method taught by Maddaloni et al. utilizes the exact same materials and method steps as are recited in the rejected claims, the method taught by Maddaloni et al. is presumed to produce the same end result as the claimed method, including results not recited in the claims.

Applicants further maintain that Maddaloni in fact teaches away from the invention in his discussion of the problem of cytotoxicity of RIPs on host cells. (p.400, column 1, first full paragraph). Applicants remind The Examiner that a prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *WL. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d

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1540 (Fed Cir. 1983, cert denied, 469 U.S. 851 (1984)). Applicants point out that Maddaloni even presents possible solutions for preventing cytotoxicity, which is the opposite goal of the present invention, while retaining the ability to protect plants from pathogens. ( p. 400, column 1, line 23, through column 2, line 2). (reply pages 10- 11).

In response to Applicants' argument that Maddaloni et al. teaches away from the invention, the Examiner maintains that Applicants' argument is inapposite to the outstanding rejection, which asserts that Maddaloni et al. in fact anticipates the rejected claims under 35 U.S.C. 102(b).

### ***Claim Rejections - 35 USC § 103***

Claims 39-40 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maddaloni et al. (Transgenic Research, 1997, Vol. 6, No. 6, pages 393-402) in view of Hey et al. (Plant Physiology, 1995, Vol. 107, pages 1323-1332) and Boston et al. (US 5,332,808 issued July 26, 1994, Applicant's IDS), for the reasons of record.

Applicants' arguments filed March 22, 2005 have been fully considered but they are not persuasive.

As discussed above, Applicants maintain that Maddaloni simply fails to disclose, or even suggest, the use of a inducible promoter to achieve specific localized expression of maize type 3 ribosome inactivating protein at and/or adjacent to a target site in a host plant to induce plant cell death at that target site. Applicants maintain that Maddaloni teaches increased tolerance against infection from a soil-born fungal pathogen by directing ribosome inactivating protein activity toward the invading pathogen, i.e., to induce fungal cell death. As discussed above, Applicants also maintain that Maddaloni in

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fact teaches away from the invention in his discussion of the problem of cytotoxicity of RIPs on host cells. (p.400, column 1, first full paragraph). Applicants also point out that there is absolutely no such disclosure, or suggestion, to be found in Maddaloni to support the Examiner's statement that plant cell death is desirable, and Applicants maintain that Maddaloni in fact suggests methods for avoiding plant cell death. ( p.400, column 1, line 19, through column 2, line 2). (reply pages 11-12)

In response to Applicant's argument that Maddaloni et al. fail to show certain features of Applicant's invention, it is noted that the features upon which Applicant relies (i.e., the use of a inducible promoter to achieve specific localized expression of maize type 3 ribosome inactivating protein at and/or adjacent to a target site in a host plant to induce plant cell death at that target site) are not recited in the rejected claim(s).

Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In the instant case Maddaloni et al. do not teach away from the claimed invention because Maddaloni et al. anticipate what is claimed. Further, because the method taught by Maddaloni et al. utilizes the exact same materials and method steps as are recited in the rejected claims, the method taught by Maddaloni et al. is presumed to produce the same end result as the claimed method.

With regard to the Hey and Boston references, Applicants assert that neither reference makes up for the deficiencies of Maddaloni, as neither reference discloses, teaches, or suggests the use of target tissue selective localized expression of a ribosome inactivating protein for induction of plant cell death. (reply page 12)

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With respect to Hey et al. and Boston et al., neither reference need disclose, teach, or suggest the use of target tissue selective localized expression of a ribosome inactivating protein for induction of plant cell death, in order to render the claimed invention obvious, as the use of target tissue selective localized expression of a ribosome inactivating protein for induction of plant cell death is not required by the rejected claims. Furthermore, Hey et al. and Boston et al. were not cited for their teachings with respect to localized expression of a ribosome inactivating protein. Hey et al. was cited for teaching a biologically active recombinant mature maize RIP comprising an  $\alpha$  domain and a  $\beta$  domain arranged contiguously, and Boston et al. was cited for teaching the use of a nos terminator in a plant expression construct.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 45, 51, 52 and 53, and claim 54 dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 45, 51, 52 and 53 are indefinite in the recitation of "stringent hybridization conditions". It is unclear what conditions would yield the claimed nucleic acid molecules because those skilled in the art define "stringent" hybridization conditions differently. It is suggested that the claims be amended to recite specific hybridization conditions in order to overcome the rejection.

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**Remarks**

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins  
Examiner  
Art Unit 1638

CC

*Cynthia Collins*  
7/6/05